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09/854,864	05/14/2001	Lars Eyde Theill	A-686B	9916

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U.S. Patent Operations/ TJG
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EXAMINER
HADDAD, MAHER M

ART UNIT	PAPER NUMBER
1644	11

DATE MAILED: 07/16/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/854,864	Applicant(s) THEILL ET AL.	
	Examiner Maher M. Haddad	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2001 and 02 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,4 and 22-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,4 and 22-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4)☐ Interview Summary (PTO-413) Paper No(s). _____ .
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

~~1. Claims 3-4 and 22-24 are pending.~~

2. Applicant's election of Group VI, claims 3-4 and 14-24, (now claims 3-4 and 22-24) in Paper No. 10, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Since the elected species, the TACI/BCMA extracellular consensus sequence (SEQ ID NO:13), is now found to be free of the prior art, the prior art search has been extended to cover the extracellular region of TACI (SEQ ID NO: 15).

3. Claims 3-4 and 22-24 are under examination as they read on a method of inhibiting TACI activity, BCMA activity or both in mammal comprises adininstering a specific binding partner for APRIL and further comprising adminitering a specific binding partner for AGP-3 as they read on SEQ ID NO:13 and SEQ ID NO:15.

4. Claim 23 is objected to because it is dependent on non-elected claims 7, 8 and 9 and should be written as an independent claim.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claim 22 is indefinite for being in improper format. The word "or" should be inserted before the last member of the Markush Group. Also, a comma should separate related materials rather than a period. In addition, in claim 22(b) a parenthesis is missing in the recitation of "(SEQ ID NO:6".

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 3-4 and 22-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting TACI activity, BCMA activity, or both in a mammal, which comprises administering the TACI/BCMA extracellular consensus sequence (SEQ ID NO:13), the extracellular region of TACI (SEQ ID NO:15), the extracellular region of BCMA (SEQ ID NO:6), the consensus region of TACI (SEQ ID NO: 16) and the consensus region of BCMA (SEQ ID NO: 7) does not reasonably provide enablement for a method for inhibiting TACI activity, BCMA activity, or both in a mammal, which comprises administering any binding partner for APRIL in claim 3; said method further comprising administering any binding partner for AGP-3 in claim 4; wherein the specific binding partner comprises any sequence recited in claim 22. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The specification disclosure does not enable one skilled in the art to practice the invention without any undue amount of experimentation.

Besides SEQ ID NO: 6-7, 13 and 15-16, the specification fails to provide any guidance as to how to make and how to use any "binding partner for APRIL" or any "binding partner for AGP-3".

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

Applicant has not provided sufficient biochemical information that distinctly identifies such "binding partner" other than SEQ ID NOS: 6-7, 13 and 15-16. While any "binding partner" may have some notion of high "affinity", claiming biochemical molecules by such properties fails to provide sufficient guidance and direction as to how the skilled artisan can make such partners, commensurate in scope with the claimed invention. The specification (page 37, lines 25-27) fails to provide any guidance on how to make any antibody, any peptide, any Fc-fusion peptide, or any receptor fragments that can be used to inhibit TACI activity, BCMA activity, or both in a mammal.

The term "comprises" in claim 22 is open-ended, it expand the amino acid sequence of SEQ ID NOS: 6-7, 13 and 15-16 to include additional non disclosed amino acids outside of the "the TACI/BCMA extracellular consensus sequence" and "the extracellular region

of TACI". There is insufficient guidance as to which amino acid segments within the polypeptide can be unique and retain a distinct functional capability of TACI/BCMA extracellular consensus sequence. Ngo *et al* teach that the amino acid positions within the polypeptide/protein that can tolerate change such as conservative substitution or no substitution, addition or deletion which are critical to maintain the protein's structure will require guidance (see Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). *In re Fisher*, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Since the amino acid sequence of a polypeptide determined its structural property, predictability of which amino acid fragment can retain the functional capabilities of the TACI/BCMA extracellular consensus sequence requires knowledge of, and guidance with regard to, which segments in the polypeptide's sequence contribute to its function.

Minor structural differences among structurally related compounds or compositions can result in substantially different biological activities. Therefore, structurally unrelated compounds comprising any "binding partner" would be expected to have greater differences in their activities.

Therefore, there is insufficient direction or objective evidence as to how to make and to how to use any binding partner which inhibits TACI activity, BCMA activity or both for the number of possibilities associated with the myriad of direct and indirect effects associated with various "binding partners" and, in turn, as to whether such a desired effect can be achieved or predicted, as encompassed by the claims.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

9. Claims 3-4 and 22-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of a method of inhibiting TACI activity, BCMA activity, or both in a mammal, which comprises administering TACI/BCMA extracellular consensus sequence (SEQ ID NO:13), the extracellular region of TACI (SEQ ID NO:15), the extracellular region of BCMA (SEQ ID NO:6), the consensus region of TACI (SEQ ID NO: 16) and the consensus region of BCMA (SEQ ID NO: 7).

Applicant is not in possession of a method for inhibiting TACI activity, BCMA activity, or both in a mammal, which comprises administering any binding partner for APRIL in claim 3; said method further comprising administering any binding partner for AGP-3 in claim 4, wherein the specific binding partner comprises any sequence recited in claim 22.

Applicant has disclosed only TACI/BCMA extracellular consensus sequence (SEQ ID NO:13), the extracellular region of TACI (SEQ ID NO:15), the extracellular region of BCMA (SEQ ID NO:6), the consensus region of TACI (SEQ ID NO: 16) and the consensus region of BCMA (SEQ ID NO: 7); therefore, the skilled artisan cannot envision all the contemplated partner of APRIL or AGP-3 possibilities recited in the instant claims. Consequently, conception cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was

not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

10. Claims 3-4 and 22-23 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 5,969,102, as is evidenced by Ware (J.Exp. Med 192:F35-F37, 2000).

The `102 patent teaches methods of inhibiting TACI activity by various means such as the free N-terminal extracellular domain of TACI (claimed SEQ ID NO:15) (see sequence alignment in particular) and the expression of a non-functional extracellular domain lacking a signal transduction domain, e.g., GPI-linked N-terminal TACI (column 40, lines 45-57 in particular) in human or any animal (column 42, lines 7-13 in particular).

While the prior art disclosure is silent as to the "the extracellular region of TACI (SEQ ID NO:15) binds to APRIL and AGP-3" per se; the method of treatment, patients and the product used in the method are the same as the claimed invention. Therefore, the binding of extracellular region of TACI (SEQ ID NO:15) ~~binds~~ to APRIL and AGP-3 is considered an inherent property.

Further, as is evidenced by Ware, that BCMA and TACI bind APRIL and BAFF (AGP-3) with relatively high affinity. Ware concluded that direct intervention targeted at BAFF, APRIL or both is readily accomplished with the soluble decoys of TACI or BCMA. This could be the pharmaceutical version of the "two for the price of one" (page F37, left column, last paragraph in particular).

The reference teachings anticipate the claimed invention.

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,969,102, as is evidenced by Ware, in view of U.S. Patent No. 6,165,745.

The teachings of `102 patent and Ware have been discussed, supra.

The claimed invention differs from the reference teachings.only by the recitation of the vehicle is an Fc doman in claim 24.

The `745 patent teaches that the large scale production of immunoglobulin Fc-hinge or Fc domains linked to other proteins or drugs also has potential for immunotherapy, such chimaeric proteins produced have the advantage of prolonged half lives (column 16, lines 5-10 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to covalently link Fc domains taught by the `745 patent to the GPI domain of N-terminal TACI and use in the methods of inhibiting TACI activity in a mammal as taught by the `102 patent.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because such chimaeric proteins produced have the advantage of prolonged half lives.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.
Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
July 15, 2002

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